Hypoxia and Cyanosis

INTENDED LEARNING OBJECTIVES (ILOs)

By the end of this lecture the student will be able to:

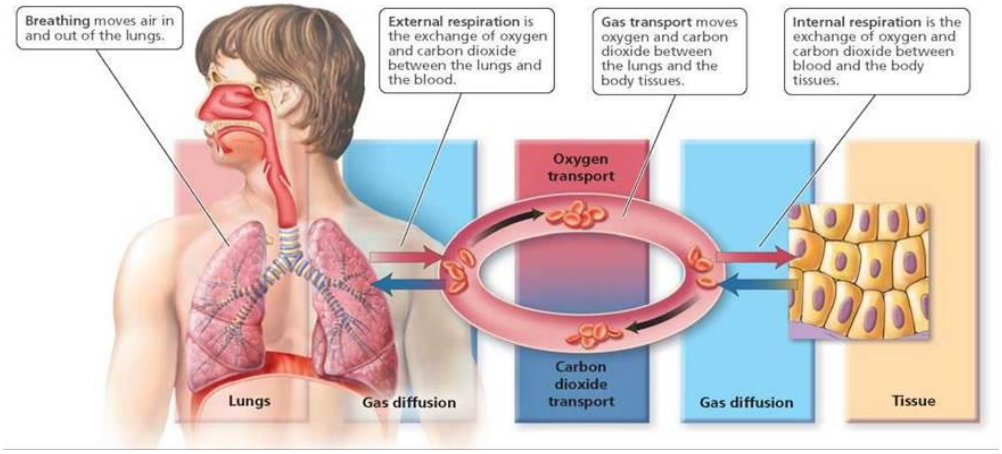
- ✓ Define hypoxia and describe its four principal forms.
- ✓ Explain the effect of each type of hypoxia on PaO_2, PvO_2, O_2 content and % saturation of HB with O_2.
- ✓ Mention the effectiveness of O_2 therapy in treatment of hypoxia.
- ✓ Define cyanosis and describe its threshold.
- ✓ Explain central and peripheral cyanosis.
- ✓ Explain types of hypoxia associated with cyanosis.
- ✓ Apply the information studied in this section to solve a clinical problem or explain clinical case.

Hypoxia:

Definition: Lack of O_2 ***at tissue level***.

Types: there are 4 types of hypoxia.

1. Hypoxic hypoxia.
2. Anemic hypoxia.
3. Stagnant hypoxia.
4. Histotoxic hypoxia.



https://schoolbag.info/biology/humans/19.html

Hypoxic hypoxia:

Definition: It is due to inadequate oxygenation of the arterial blood i.e. the PO_2 of the arterial blood is reduced (Hypoxemia).

Because the amount of oxygen that will combine with hemoglobin is mainly determined by the PO_2, when PO_2 is decreased oxygen delivery to the tissues will decrease.

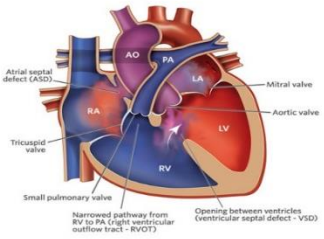
It is the most common type of hypoxia.

Causes:

a) **Decrease the O_2 tension in atmosphere**: as in high altitude the Barometric pressure is decreased which decreases the PO_2 of inspired air and of alveolar air (PAO_2). Equilibration of O_2 across the alveolar/pulmonary capillary barrier is normal, and systemic arterial blood achieves the same **(lower)** PO_2 as alveolar air. Because PAO_2 and PaO_2 are nearly equal, **the A - a gradient** (alveolar-arterial gradient) **is normal**. Alveolar carbon dioxide is decreased because of the reflex increase in ventilation caused by hypoxic stimulation.
b) **Impaired ventilation (hypoventilation):** It is characterized by a reduced PAO_2, PaO_2 and an increased $PaCO_2$ since alveolar ventilation is reduced. There is **no increase in A-a gradient** as equilibration of O_2 across the alveolar-pulmonary capillary barrier is normal.
    - Respiratory center depression e.g. morphine poisoning
    - Respiratory muscle diseases: myopathy or poliomyelitis
    - Chest wall deformities
    - Obstructive diseases: COPD, asthma
    - Restrictive diseases (non-compliant lung): lung fibrosis and Asbestosis
c) **Impaired diffusion:** It occurs due to a **failure of PO_2** in the pulmonary capillary blood **to equilibrate** with alveolar gas. Most of abnormalities in diffusion are too mild to cause hypoxemia unless the patient is **exercising** or **has extremely abnormal alveolar-capillary barrier**. The lung diffusion capacity is decreased, and the **A-a gradient is increased.**
    - Decrease pulmonary surface area e.g. patient with emphysema.
    - Increase pulmonary membrane thickness e.g. pneumonia, fibrosis, sarcoidosis, asbestosis, pulmonary congestion and pulmonary edema.
d) **Venous- arterial shunt *(Right-to-left shunt)*:**
   Occurs when mixed venous blood bypasses the gas-exchange unit and goes directly into the arterial circulation resulting in dilution of the oxygenated blood in the systemic circulation thus, reducing PaO_2 while the PAO_2 is unaffected, so, **the A-a gradient is increased.**

- **Anatomical shunt:**

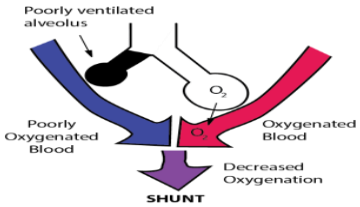
Like intrapulmonary shunts, but most anatomical shunts develop within the heart in which the non-oxygenated blood from the right side of the heart bypasses oxygenation at pulmonary capillaries and pass directly to the left side of the heart. This is seen in **tetralogy of Fallot (**cyanotic congenital heart diseases).



diseases/tetralogy-fallot

- **Physiological Shunt (intrapulmonary shunt):**

An intrapulmonary defect in which mixed venous blood perfuses unventilated alveoli will mix with arterial blood from well-ventilated alveoli.

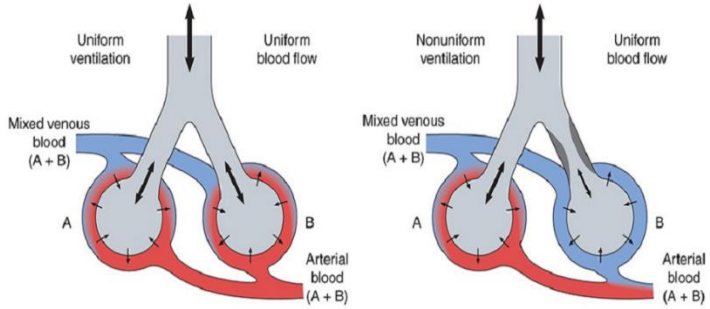


Left-to-right shunt: It is another type of shunts, and it is more common, blood pass from the left side of the heart to the right side. It is seen with several congenital abnormalities, including patent ductus arteriosus (PDA), atrial septal defect, and ventricular septal defect. ***Left-to-right shunts do not decrease PaO_2*** since oxygenated blood is returning to the right side of the heart, raising its PO_2.

e) **Ventilation perfusion imbalance**

- is by far the **most common cause of hypoxemia** and many lung diseases, including chronic obstructive pulmonary disease, that cause hypoxia in this way. When ventilation is not in balance with perfusion e.g. when alveolar ventilation is distributed unevenly between the two alveoli and blood flow is equally distributed. the under-ventilated alveoli (B) will have low alveolar PO_2, and the blood coming from it will be not fully saturated, whereas the overventilated alveoli (A) will have high alveolar PO_2 and the blood coming from it is greatly saturated.

The unsaturation of the hemoglobin of the blood coming from B is not fully compensated by the slightly greater saturation of the blood coming from A. Consequently, the arterial blood is less saturated.



Ganong's Review of Medical Physiology, 2016

Criteria:

- ✓ ***Decrease oxygen tension (PO_2)*** in arterial blood will lead to ***decrease Hb saturation with O_2*** and ***decrease O_2 content***.

- ✓ ***In Venous*** blood **all *O_2 tension*, *Hb saturation*** and ***O_2 content*** are ***below normal*** as oxygen is extracted from the already hypoxic arterial blood.

Anemic Hypoxia:

Definition: Hypoxia due to lack of functioning Hb (capable of carrying O_2) while the arterial PO_2 is normal.

Causes:

a) Quantitative: all types of anemia.
b) Qualitative:
   - CO poisoning
   - Met Hemoglobin
   - Sulf Hemoglobin

N.B. In Anemic Hypoxia the manifestation is not severe due to increase 2,3 DBG in case of anemia ***Except*** with **Hb deficiency is high** or during **EXERCISE** Hypoxia effect might be severe because Of the Limited activity to increased O_2 delivery to active tissue.

Criteria:

- ✓ Decrease functioning Hb will lead to ***decrease arterial O_2 content***, but ***both arterial O_2 tension*** and ***Hb saturation with O_2 are normal***.
- ✓ ***In Venous*** blood **all *O_2 tension*, *Hb saturation*** and ***O_2 content*** are ***below normal*.**

CO poisoning (special type of anemic hypoxia)

CO is formed by incomplete combustion of carbon generated from a malfunctioning space heater or from car exhaust, car operating in poorly ventilated areas. It is toxic as:

- CO binds to Hb (carboxyhemoglobin (COHgb)) at same site as O_2 decrease O_2 loading.
- Hb has affinity to CO 210 time as O_2.
- CO cause shift of the O_2-Hb dissociation curve to the left decrease O_2 unloading.
- CO breaks down slowly.

Cherry-red skin color produced by CO poisoning.

https://lonegp.wordpress.com/2018/07/16/carbon-monoxide/

Symptoms and Signs:

Patient experience headache, nausea, and dizziness. His skin and mucous membrane appear ***cherry red*** in color.

N.B. *There is little stimulation of respiration, since in the arterial blood, PO_2 remains normal and the carotid and aortic chemoreceptors are not stimulated.*

Oxygen saturation as measured with conventional pulse oximeter is normal (as it does not differentiate between oxygenated hemoglobin and carboxy hemoglobin). Thus, it is imperative that the clinician recognize a potential case of carbon monoxide poisoning and order an arterial blood gas analysis for oxygen saturation measurement with the use of a carbon monoxide oximeter (to identify the proportions of oxyHb, deoxyHb, COHgb levels).

Criteria:

- ✓ Same as anemic hypoxia but with ***low O_2 saturation.***

Treatment:

- Termination of exposure
- Artificial respiration
- O_2 therapy: Hyperbaric O_2 or 95% O_2 +5% CO_2 to stimulate respiration
- Exchange transfusion
- Complete rest for several hours.

Stagnant Hypoxia (hypoperfusion):

Definition: Hypoxia due to inadequate blood flow or slow circulation i.e. adequate O_2 is not delivered to it tissue despite a normal PO_2 and hemoglobin concentration.

Causes:

a) Generalized: due to congestive heart failure or circulatory shock.
b) Localized: due to vascular obstruction.

Criteria:

- ✓ In this type arterial ***O_2 tension***, ***Hb saturation*** and ***O_2 content*** are ***normal,*** the O_2 delivery to tissue is low due to decrease in the flow**.**
- ✓ ***In Venous*** blood **all *O_2 tension*, *Hb saturation*** and ***O_2 content*** are ***below normal*.**

Histotoxic Hypoxia:

Definition: It is due to inability of tissue to utilize O_2, despite the amount of O_2 delivered to a tissue is adequate.

Causes:

a) Cyanide poisoning: inhibit cytochrome oxidase.
b) Alcohol and narcotics

Criteria:

- ✓ In this type arterial ***O_2 tension*, *Hb saturation*** and ***O_2 content*** are ***normal,*** the O_2 delivery to tissue is normal but the cells can't utilize the O_2.

- ✓ ***In Venous*** blood **all *O_2 tension*, *Hb saturation*** and ***O_2 content*** are ***above normal*.**

Treatment of cyanide poisoning:

- Injection of **methylene blue or nitrite,** forming methemoglobin, which then reacts with cyanide to form **cyanmethemoglobin**, a nontoxic compound. Which is removed by liver or kidney.

Clinical manifestation of hypoxia:

- ➢ **Moderate hypoxia**

  1) On brain: Headache, impaired judgment, pain and drowsiness.

  2) On circulation: Increase heart rate and arterial blood pressure.

  3) On respiration: Increase respiratory rate.

  4) On GIT: Nausea and vomiting.

- ➢ **Severe hypoxia**

  PO_2 less than 20 mmHg loss of conscious in about 20 seconds and death in about 4-5 minutes.

O_2 therapy in different types of hypoxia:

O_2 is highly beneficial in:

- ✓ Hypoxic hypoxia due to decrease atmospheric PO_2, hypoventilation and impaired diffusion.
- ✓ CO poisoning

*O_2 therapy will increase both **chemically combined** and **physically dissolved** O_2.*

O_2 is less beneficial in:

- o Hypoxic hypoxia due to venous to arterial shunt. As the deoxygenated venous blood does not have the opportunity to get to the lung to be oxygenated.
- o Anemic hypoxia due to low Hb content.
- o Stagnant hypoxia.

*O_2 therapy will increase **physically dissolved** O_2 only.*

O_2 is not beneficial in:

- ☒ Histotoxic hypoxia

O_2 toxicity:

Administration of 100% O_2 has been found to have toxic effects. The toxicity is to be due to the production of reactive oxygen species including superoxide anion (O_2^-) and H_2O_2. The symptoms develop is dependent on the duration of administration and speed of these symptoms is proportional to the pressure at which the O_2 is administered

- Administration of 80-100% O_2 for
  - 8 hours irritate the respiratory tract e.g. nasal congestion, sore throat, and coughing.
  - from 8 to 48 hours damage to lungs
  - above 48 hours damage to CNS
- Administration of O_2 to premature baby induce vasoconstriction in retinal blood vessels (retrolental fibroplasias)
- Administration of hyperbaric O_2 (100% but under high pressure) will accelerate the onset of toxicity.

		Hypoxic hypoxia	Anemic hypoxia	Stagnant hypoxia	Histotoxic hypoxia
Arterial	PO_2	↓↓	Normal	Normal	Normal
	Content	↓↓	↓↓	Normal	Normal
	% saturation	↓↓	Normal (low in CO poisoning)	Normal	Normal
Venous	PO_2	↓↓	↓↓	↓↓	↑↑
	Content	↓↓	↓↓	↓↓	↑↑
	% saturation	↓↓	↓↓	↓↓	↑↑
Cyanosis		Present	Absent	Present	Absent
O_2 therapy		Beneficial in all except venous to arterial shunt ↑Both chemical and physically dissolved O_2	Less beneficial except with CO poisoning ↑ only physically dissolved O_2	Less beneficial ↑ only physically dissolved O_2	Not beneficial

Cyanosis

Definition: Bluish discoloration of skin and mucous membrane due to presence of excess reduced Hb in capillaries.

Threshold for cyanosis: more than 5g reduced Hb/100ml capillary blood

Causes:

- Hypoxic hypoxia
- Stagnant hypoxia
- Asphyxia
- Polycythemia
- Moderate cold

Seen in:

- Nail bed
- Mucus membrane
- Ear lobes

Types:

Features	Central cyanosis	Peripheral cyanosis
Mechanism	**(Hypoxic hypoxia)** Inadequate oxygenation of systemic arterial blood due to respiratory defect or circulatory defect e.g. cardiac right-to-left shunts (e.g. tetralogy of Fallot.	**(Stagnant hypoxia)** Low output states as in congestive hart failure, sluggish peripheral circulation e.g. vascular obstruction or exposure to moderate cold (decrease blood flow to extremities)
Sites to look	All over the body Tongue is involved	Localized to the area of decrease blood flow Tongue is **not** involved Fingertips, nail bed, extremities
Warming extremities	No change	Disappears
		

Relation between Hypoxia and cyanosis:

The intensity of cyanosis is not a reliable sign for the degree of hypoxia (both not run in parallel)

1. Cyanosis does not occur with some types of hypoxia as

a. *Anemic hypoxia:* the total amount of Hb is low
b. *Histotoxic hypoxia:* no reduce Hb.
c. *CO poisoning:* due to the cherry red color of CO-Hb.

2. Person with excess red blood cells, as in polycythemia, has greater liability to become cyanotic, even under normal conditions, because he has great excess hemoglobin that can become deoxygenated.

Factors modify the color of the cyanosis:

1. Blood composition
   Total amount of Hb: in anemia (cyanosis rarely appears), in polycythemia (cyanosis easily appear)
   Amount of reduced Hb
2. Skin
   Thickness: cyanosis appears in thin skin e.g. nail beds, ear lobes.
   Pigmentation: cyanosis is masked in dark races.

SUGGESTED TEXTBOOKS

1. Ganong's Review of Medical Physiology, twenty-fifth edition 2016, McGraw-Hill Education, chapter 35, from page 646 to 653

2. Guyton and Hall textbook of medical physiology, thirteenth edition 2016, Elsevier, chapter 43, from page 554 to 556